REMARKS

Claims 1-2, 5-11, 13-22, 24-27, 30-34 and 36-37 were rejected. Claims 5, 17-21, 31-32 and 37 are herein cancelled. The other claims are amended. Claim 38 is new and is supported by original claim 34. The amendments and new claim do not introduce new matter. Amended claim 1 is supported at p. 20, Example 2A at lines 7 et seq. and from original claims 5 and 9. Amended claim 16 is supported by original claim 16 and at pp. 18-19, Example 1D and page 1, under Field of the Invention.

35 USC § 103

Claims 1-2, 5-11, 13-22, 24-27, 30-34 and 36-37 were rejected under 35 USC § 103(a) as being unpatentable over Ghosal (U.S. Patent No. 6,362,167) in view of Ghosal (U.S. Patent No. 6,440,436) as evidenced by Pushpangadan et al. (U.S. Publication No. 2003/0185913) and in further view of Boynton et al. (U.S. Patent No. 5,087,623). Applicant traverses the rejection.

The Examiner discussed the cited prior art, not in the present Office Action, but in the Office Action of August 22, 2008. In response, Applicant argued that the Examiner's conclusions were not supported. In light of the amended claims, Applicant resubmits the errors in the Examiner's logic as they pertain to the amended claims.

Claim 1 is directed to a phenolic antioxidant-chromium complex that has no pro-oxidation activity and wherein the phenolic antioxidant is in a purified tannin fraction of plant origin. In a similar manner, claim 14 is directed to a phenolic antioxidant-chromium complex that has no pro-oxidation activity and wherein the phenolic antioxidant comprises oxygenated dibenzo-α-pyrone (DBP) or a DBP conjugate and fulvic acid. The complexes are therapeutic for hyperglycemia.

In the previous office action, the Examiner stated that Pushpangadan discloses that herbal health compositions can be used to control blood sugar levels in patients with diabetes, citing to page 2, para. [0014] of Pushpangadan. In this office action the Examiner repeated the statement. This was a mischaracterization of the prior art. Referring to paragraph [0014], Pushpangadan did not disclose that *any and all* herbal health compositions can be used to control blood sugar levels, only the particular herbal health composition that is the Pushpangadan formulation, and

this formulation did not contain any shilajit or *P. emblica*. Unlike the Pushpangadan formulation, the presently claimed products require ingredients obtainable from shilajit and/or *P. emblica* and the present application, but not Pushpangadan, disclose that these ingredients are useful to treat hyperglycemia.

The Examiner continued the analysis with US'167 which teaches *E. officinalis* fruit has an antioxidant activity without pro-oxidant side reactions and US'436 which teaches purified shilajit composition comprising dibenzo-α-pyrone and fulvic acids. The Examiner also stated that Pushpangadan discloses commercial herbal anti-diabetic products containing shilajit and *E. officinalis*. The Examiner then concluded, improperly, "Thus, the extract from the fruit of the *E. officinalis* plant and purified shilajit can be used to treat hyperglycemia in patients with diabetes." This conclusion was improper because nowhere in any of the cited references was it disclosed that treatment of hyperglycemia could be targeted to *E. officinalis* or shilajit. The composition disclosed in Pushpangadan contained some 20 different herbal ingredients with no disclosure of what kind of activity any of the individual ingredients was contributing, whether it be aroma, taste or healthful activity. Further, Pushpangadan did not disclose that the composition contained the fruit portion of *E. officinalis* or a purified shilajit fraction. In fact, the Pushpangadan description of the Madhumeh Amrit product which contained a total of 20 herbal or folk ingredients, specified that it was the leaves, seeds or flowers that were to be used for certain plants but made no such targeted suggestion for *Phyllanthus emblica* (aka *E. officinalis*). Thus the person of ordinary skill in the art would have had no way of ascertaining that the fruit of the *E. officinalis* plant was a targeted portion. The Examiner was working from hindsight benefit of the present application's disclosure to draw that conclusion. In similar manner, Pushpangadan's description of the Madhumeh Amrit product did not state that a purified fraction was used from the shilajit. Hindsight, again.

With regard to the present amended claims, the Examiner's conclusion was improper for two more reasons. First, Pushpangadan does not disclose that a purified tannin fraction of *E. offinalis* has anti-diabetic properties or treats hyperglycemia. Nor does it disclose that a purified fraction of Shilajit containing DBP and fulvic acids has anti-diabetic properties or treats hyperglycemia. The person of ordinary skill would have had no way of knowing from

Pushpangadan, that *E. officinalis* and shilajit could yield, through chemical treatment, purer fractions that had this activity. Furthermore, even in combination with the disclosures of US'167 and US'436 of how to obtain antioxidant fractions, the person of ordinary skill would have had no way of knowing that those fractions would be therapeutic for hyperglycemia because none of the cited prior art gave that information. For this reason, the combined prior art did not teach a therapeutic product for hyperglycemia that is a phenolic-antioxidant-complex that has no pro-oxidation activity and wherein the phenolic antioxidant is in a purified tannin fraction of plant origin or the phenolic antioxidant that comprises oxygenated dibenzo-α-pyrone (DBP) or a DBP conjugate, and fulvic acid from a purified shilajit.

Furthermore, since the person of ordinary skill would have had no reason to believe that the particular fractions as claimed had any therapeutic properties in regard to hyperglycemia, the ordinary skilled person would have had no reason to combine Boynton's chromium picolinate with those particular fractions. According to the Examiner's logic, it was the fact that it was known that both Boynton's chromium picolinate and the antioxidants from *P. emblica* and shilajit are therapeutic for hyperglycemia that would have motivated one of ordinary skill in the art to combine them. However, there was no such teaching in the cited prior art with regard to *P. emblica* and shilajit. Thus, there is no logical progression in the Examiner's conclusion that "the motivation to combine the extracts of [US'167] and [US'436] as evidenced by Pushpangadan et al to the chromic picolinate compound of Boynton et al is that the extracts from Phyllanthus emblica fruit and purified shilajit of [US'167] and [US'436] and the chromic picolinate compounds of Boynton et control high blood serum glucose levels." (Office Action, p. 4).

Another reason that the rejection is improper relates to the Examiner's reiteration of the argument that Pushpangadan is cited for the teaching that commercial herbal anti-diabetic products containing Shilajit and *Phyllanthus emblica* are available. However, the meaning of the term "anti-diabetic" as used by Pushpangadan was never made clear. There is certainly no teaching that these products control blood glucose levels. Only Pushpangadan's own product was disclosed to control blood glucose and that product had no *P. emblica* or shilajit. Furthermore, since Applicant has shown (Amendment arguments submitted September 10, 2008)

that Pushpangadan teaches that the products don't ameliorate the health of diabetics, there is no evidence what these "anti-diabetic" products do. Just because the products are marketed with the terminology "anti-diabetic" on the label, does not constitute any type of showing that these products control blood glucose levels. Applicant has already provided evidence that Pushpangadan taught that the products are "without a suitable balanced nutritional composition to ameliorate the general health of diabetics." Since there is no teaching that the products control blood glucose, the Examiner erroneously relied on Pushpandagan for a fact that is simply not there. The only herbal product that Pushpangadan taught lowers blood glucose, was the Pushpangadan formulation, which contains neither shilajit nor *Phyllanthus emblica* (see Applicant's argument submitted Sept. 10, 2008, p. 7 and Pushpangadan, para. [0014],[0017] and [0018]). For this reason, the Examiner's statement that according to Pushpangadan et al. and Boynton et al., both the extracts from Phyllanthus emblica fruit and purified shilajit and chromium are used to control high blood serum glucose levels is erroneous and the Examiner's conclusion about the obviousness of the invention is without substantiation. For these reasons, it is respectfully requested that the rejection be reconsidered and withdrawn.

Applicant had also argued previously that secondary considerations in the form of long felt but unsolved need support the non-obviousness of the invention. Specifically, Applicant argued that it was recognized that chromium (III), as a dietary supplement, is converted to toxic chromium (VI) by spontaneous systematic oxidation and hence induces delayed toxicity and that it was recognized that safer alternatives were needed. This was not mere attorney argument, but was described in the present specification at page 5, Description of Prior Art, first paragraph. In response, in the present office action, the Examiner stated that there was no evidence of a need that was "a persistent one that was recognized by those of ordinary skill in the art." In response to the Examiner's statement, Applicant submits as Exhibit 1 the Abstract of Bagchi et al, Toxicology, 2002; 180(1):5-22, which makes reference to the large number of studies that demonstrated that chromium (VI) induces oxidative stress, DNA damage, apoptotic cell death and altered gene expression. (Abstract). Bagchi et al also taught that the popular dietary supplement chromium (III) picolinate produces oxidative stress and DNA damage and Bagchi et al makes reference to studies that have implicated chromium picolinate toxicity in renal

impairment, skin blisters, anemia, hemolysis, tissue edema, liver dysfunction, neuronal cell injury, impaired cognitive, perceptual and motor activity, enhanced production of radicals, chromosomal aberration, depletion of antioxidant enzymes, and as being mutagenic. (Abstract). Thus, Applicant reasserts that there was a recognized and persistent need for safer alternatives to the known dietary supplements for chromium. In response to this need, an object of the claimed invention was to provide a composition for treating diabetes or glucose intolerance by employing a safe and effective phenolic antioxidant-chromium complex, without pro-oxidation activity. In light of this evidence showing a persistent and recognized long-felt need, the Examiner is required to show that this secondary consideration of obviousness has been weighed into the determination of the patentability of the invention. As stated by the Federal Circuit Court, "As we have repeatedly emphasized, evidence relating to secondary considerations 'constitutes independent evidence of nonobviousness' and can be quite instructive in the obviousness inquiry." Süd-Chemie, Inc. v. Multisorb Techs., Inc., (Fed. Cir., 08-1247, January 30, 2009).

In view of the foregoing, Applicants submit that all pending claims are in condition for allowance and request that all claims be allowed. The Examiner is invited to contact the undersigned should he believe that this would expedite prosecution of this application. It is believed that no fee is required. The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,

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EXHIBIT 1

1: Toxicology. 2002 Oct 30;180(1):5-22.

Comment in:
Toxicology. 2003 Apr 15;186(1-2):171-3; author reply 175-7.

Cytotoxicity and oxidative mechanisms of different forms of chromium.

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Chromium exists mostly in two valence states in nature: hexavalent chromium [chromium(VI)] and trivalent chromium [chromium(III)]. Chromium(VI) is commonly used in industrial chrome plating, welding, painting, metal finishes, steel manufacturing, alloy, cast iron and wood treatment, and is a proven toxin, mutagen and carcinogen. The mechanistic cytotoxicity of chromium(VI) is not completely understood, however, a large number of studies demonstrated that chromium(VI) induces oxidative stress, DNA damage, apoptotic cell death and altered gene expression. Conversely, chromium(III) is essential for proper insulin function and is required for normal protein, fat and carbohydrate metabolism, and is acknowledged as a dietary supplement. In this paper, comparative concentration- and time-dependent effects of chromium(VI) and chromium(III) were demonstrated on increased production of reactive oxygen species (ROS) and lipid peroxidation, enhanced excretion of urinary lipid metabolites, DNA fragmentation and apoptotic cell death in both in vitro and in vivo models. Chromium(VI) demonstrated significantly higher toxicity as compared with chromium(III). To evaluate the role of p53 gene, the dose-dependent effects of chromium(VI) were assessed in female C57BL/6Ntac and p53-deficient C57BL/6TSG p53 mice on enhanced production of ROS, lipid peroxidation and DNA fragmentation in hepatic and brain tissues. Chromium(VI) induced more pronounced oxidative damage in multiple target organs in p53 deficient mice. Comparative studies of chromium(III) picolinate and niacin-bound chromium(III), two popular dietary supplements, reveal that chromium(III) picolinate produces significantly more oxidative stress and DNA damage. Studies have implicated the toxicity of chromium picolinate in renal impairment, skin blisters and pustules, anemia, hemolysis, tissue edema, liver dysfunction; neuronal cell injury, impaired cognitive, perceptual and motor activity; enhanced production of hydroxyl radicals, chromosomal aberration, depletion of antioxidant enzymes, and DNA damage. Recently, chromium picolinate has been shown to be mutagenic and picolinic acid molety appears to be responsible as studies show that picolinic acid alone is clastogenic. Niacin-bound chromium(III) has been demonstrated to be more bioavailable and efficacious and no toxicity has been reported. In summary, these studies demonstrate that a cascade of cellular events including oxidative stress, genomic DNA damage and modulation of apoptotic regulatory gene p53 are involved in chromium(VI)-induced toxicity and carcinogenesis. The safety of chromium(III) is largely dependent on the ligand, and adequate clinical studies are warranted to demonstrate the safety and efficacy of chromium(III) for human consumption.

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